



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/486,070	06/07/1995	JANNIS G. STAVRIANOPOULOS	ENZ-7(P)(C3)	6279

28171 7590 11/26/2004

ENZO BIOCHEM, INC.
527 MADISON AVENUE (9TH FLOOR)
NEW YORK, NY 10022

EXAMINER

MARSCHER, ARDIN H

ART UNIT	PAPER NUMBER
----------	--------------

1631

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/486,070	Applicant(s) STAVRIANOPOULOS ET AL.	
	Examiner Ardin Marschel	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3144-3286 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3144-3286 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>(1 sheet)</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Due to the below set forth new grounds of rejection the finality of the office action, mailed 4/7/04, is hereby withdrawn. Also, due to said withdrawal of finality the Notice of Appeal, filed 6/30/04, is deemed moot. The amendment, filed 6/30/04, has been entered.

Applicants' arguments, filed 6/30/04, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

NEW MATTER

Claims 3147-3150, 3164-3166, 3170, 3171, 3175-3178, 3192-3194, 3198-3245, 3248-3251, 3265, 3266, 3269, 3270, and 3278 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

NEW MATTER has been amended into the claims via claim 3147 which cites the following solid supports which have not been found as filed: "a plate", "depressions", "beads", "a set of plates", "a set of...depressions", or "a set of...beads". The closest citation to these is set forth in the bridging paragraph between pages 13 and 14 as filed which cites plastic or glass wells which are not the generic wells as in instant claim

Art Unit: 1631

3147. This citation also cites "arrangements of wells, tubes or cuvettes" which includes an arrangement limitation which is more limited than the above cites sets because the sets of claim 3147 lack any arrangement limitation(s) and thus contain NEW MATTER due to broadening to sets vs. arrangements. On page 16, lines 9-14, cites a glass plate with an array of depressions or wells but not the generic plate or plates as now set forth in claim 3147 nor depressions or wells without their presence in a glass plate as now set forth in claim 3147. On page 23, line 17, conventional microtiter well plates are set forth but not the generic plate or set of plates as now set forth in instant claim 3147. Open plate(s) incubation is cited on page 23, lines 25-27, but are reasonably interpreted as describing said conventional microtiter plates and not generic plate(s) as now claimed in claim 3147. This NEW MATTER is also present in claims 3175, 3201, and 3248.

Although applicants point to a previous claim regarding the "more than one surface" type of solid support in claim 3148, a review of the instant disclosure as filed has failed to reveal any such "more than one surface" limitation. This phrase thus adds NEW MATTER compared to the instant disclosure as filed. This NEW MATTER is also present in claims 3176, 3202, 3249, 3150, and 3278.

Although applicants point to previous claims regarding the "to one of said reactive sites or binding sites" as now set forth in claim 3149, a review of the instant disclosure as filed has failed to reveal any citation regarding the particular "to one of" limitation within said phrase. This "to one of" phrase thus adds NEW MATTER compared to the instant disclosure as filed. It is acknowledged that several chemical

Art Unit: 1631

surface treatments have been disclosed as filed, such as providing alkylamine (page 16, line 1) and epoxy glue (page 23, line 3). Such surface treatment(s), however, lack any localization of nucleic acid attachment "to one of" any sites on the various surfaces or solid supports as now set forth in claim 3149 which therefore contains NEW MATTER due to said "to one of" limitation. This NEW MATTER is also present in claims 3177, 3178, 3250, and 3251.

Although applicants point to previous claims regarding claims 3164 and 3165, a review of the instant disclosure as filed has failed to reveal any written support as filed for the quantitation limitation directed to "proportional to". The specification at page 13, lines 11-28, cite quantitation of signal but not that such quantitation is via a signal which is "proportional to" an amount of label etc. This phrase thus adds NEW MATTER compared to the instant disclosure as filed. This NEW MATTER is also present in claims 3192, 3193, 3218, 3219, 3242, 3243, 3265, and 3266.

Although applicants point to a previous claim regarding claim 3165, a review of the instant disclosure as filed has failed to reveal any written support as filed for quantifiability of a label "in or from a fluid or solution" either "in" or "through" a "non-porous solid support" as now set forth in claim 3165. It is acknowledged that a fluid or solution is cited as filed as well as non-porous solid supports of various types, but not that quantifiability is practiced either "in" or "through" a non-porous support as now set forth in claim 3165. This phrase thus adds NEW MATTER compared to the instant disclosure as filed.

Although applicants point to a previous claim regarding claim 3166, a review of the instant disclosure, however, as filed has failed to reveal any written support for the "iminobiotin", "haptin", or "ligand" limitations therein. These limitations thus add NEW MATTER compared to the instant disclosure as filed. This NEW MATTER is also present in claims 3194, 3220, and 3244.

Although applicants point to previous claims regarding instant claims 3170 and 3171, a review of the instant disclosure as filed, however, has failed to reveal any written description of any "set" regarding comprising a support as set forth in either of claims 3170 or 3171. These set limitations thus add NEW MATTER compared to the instant disclosure as filed. This NEW MATTER is also present in claims 3269 and 3270.

Although applicants point to previous claims regarding instant claims 3198 etc., a review of the instant disclosure as filed, however, has failed to reveal any written description of a generic "array" comprising "various" nucleic acids. These generic various nucleic acid array limitations thus add NEW MATTER compared to the instant disclosure as filed. Applicants argue in REMARKS, filed 6/30/04, that plural sequences of analytes and DNA are cited in the specification at several instances. In response, the immobilization or fixation disclosures, including examples, as filed immobilize or fix a plurality of sequences but not specifying any variousness or differences between such pluralities unless also accompanied by requiring depressions or wells. That is, no generic description of arrays as in claim 3198 has been found as filed wherein any specificity as to sequence characterization is set forth without depressions or wells

Art Unit: 1631

required therefor. For example, in Example 1, with usage thereof in Example 2, on pages 15-18 of the specification cites arrays with depressions or wells for depositing of various denatured analytes. Instant claim 3198 lacks any corresponding limitation regarding what deposition is practiced for such various samples in contrast to the depressions or wells as in Example 1 which are reasonably interpreted as being directed to separation of such various denatured analytes into depressions or wells. In Example 3 on pages 18-19, at page 18, lines 23-25, "the analyte" (singular) was described as immobilized on an activated glass surface. This is neither an array disclosure nor cites the practice of various nucleic acids as now in claim 3198.

Applicants further argue in said REMARKS that exemplified sequences are set forth in the specification on pages 10, 20, 21, 22, and 23. Consideration of these citations reveals that no array disclosure has been found nor pointed to nor any written support for any array (singular) as claimed in claim 3198 whereon "various" nucleic acids are fixed or immobilized. Applicants further submit a Declaration from Dr. Alexander A. Waldrop, III. Consideration of said Declaration reveals that, after reviewing of scientific background and filter assay practice of the Grunstein and Hogness types, item # 9 therein discusses advantages of non-porous solid supports, none of which, however, are disclosed as filed. In said Declaration in items # 10 and 11 a NEW MATTER rejection is summarized plus Declarant's substantial experience and background. Said items 3 10 and 11 however, lack any discussion of written support contrary to this NEW MATTER rejection. Declarant then further sets forth in item # 12 array subject matter but without specifying any written description as instantly filed regarding this NEW

Art Unit: 1631

MATTER rejection. Item # 13 then summarizes various understandings but again without any description regarding written basis contrary to this NEW MATTER rejection. Then item # 14 sets forth an opinion and conclusion but only verifies that a page 16 citation in the instant specification as filed cites an array with both various nucleic acids as well as having depressions and wells. Item # 15 repeats the page 16 array disclosure wherein various nucleic acids are cited with also the array having depressions or wells and then gives a contrary opinion. This is non-persuasive in that the factual basis on said page 16 corresponds to written support for connecting various nucleic acids with an array having depressions or wells and is thus directed to the limiting written support whereas the opinion expressed in said item # 15 is an allegation which lacks any such factual support. Declarant then argues that the phrase "For example" conveys what is illustrative or exemplary of an array. This does not negate the fact that written basis for an array with various nucleic acids "only" is disclosed as filed wherein the array has depressions or wells. Declarant goes on to state that fixation or immobilization in the disclosure is not dependent on the shape or conformation of the support. In response, it has been noted above that such generic fixation or immobilization lacks any indication of "various" nucleic acids as set forth in the citation on page 16 as well as lacking in array disclosure as on page 16. Thus, the non-porous support descriptions lack any description of conception of an array type of invention. When an array invention is cited on page 16 it is only cited with various nucleic acids as well as with depressions or wells. Declarant then describes a Petrie dish plate, tube, cuvette, etc. as conventional apparatus as conveyed via Example 1. Such conveyance

Art Unit: 1631

is also lacking in written support as Example 1 does not cite any Petrie dish plate etc.

Additionally, what is conveyed in Declarant's understanding clearly is not written.

Declarant then summarizes Examples in the specification but none of them cite an array with various nucleic acids thereon independent of depressions or wells thus failing to provide written support for the generic array as claimed instantly in claims 3198 etc. In particular Example 7 is discussed regarding a conventional microtiter plate but acknowledging the fixing of "the polynucleotide analyte" (singular) thereto. Such a singular analyte fixation to a microtiter plate both provides written description for a single (not various) analyte and such a plate which is well known to contain depressions or wells. In items # 17-23 Declarant discusses the definition of analyte but fails to indicate their disposition on an array therein which also fails to provide written basis for the array of claims 3198 etc. In summary, Declarant's opinion/understanding Declaration fails to provide support for the written description of an array as now claimed in instant claims 3198-3221 which contain embodiments which are not limited to the combined limitations of various nucleic acids and depressions or wells thereon.

Claims 3222 etc. which cite an array comprising various single-stranded nucleic acids fixed or immobilized to a non-porous support having depression or wells also contains a limitation regarding cell a cell fixed *in situ* to said wells or depressions. This cell fixation *in situ* in wells or depressions or not has not been found as filed. This NEW MATTER is also present in claims 3223-3245.

VAGUENESS AND INDEFINITENESS

Claims 3144-3286 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 3170, 3171, 3269, and 3270; a set is claimed but with only one support cited therein regarding said set. Thus, the metes and bounds of the claims are vague and indefinite as to whether the set is defined by one support or whether the metes and bounds are defined by the set limitation. Additionally, there is no indication in these claims as to what would be meant if the set includes one or more item(s) other than the cited solid support. Clarification via clearer claim wording is requested.

All of the presently pending claims, either directly or indirectly via dependence from another claim cite either the phrase "directly or indirectly fixed or immobilized" or "indirectly fixed or immobilized". In the first phrase, it is unclear whether one, both, or neither of the limitations "directly" or "indirectly" applies to modify "immobilized". In the second phrase the limitation "indirectly" may or may not modify "immobilized". The lack of clear and concise metes and bounds of these phrases supports this rejection. Similar phrases, such as "indirect fixation or immobilization" in line 6 of claim 3173 also contain this unclarity.

PRIOR ART

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1631

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 3144-3148, 3151, 3155, 3156-3163, 3166-3176, 3179, 3183-3191, 3194-3197, 3246-3249, 3252, 3256-3264, and 3267-3286 are rejected under 35 U.S.C. 102(e)(2) as being clearly anticipated by Stuart et al. (P/N 4,732,847).

Stuart et al. summarizes the usage of monoclonal antibodies for distinguishing DNA-RNA hybrids on a solid surface as disclosed in the abstract. The sample nucleic acid being detected is described in Stuart et al. as being inclusive of detection of specific sequences "from a wide variety of sources" as cited in column 2, lines 30-33. In column 2, lines 48-53, the detection of both naturally occurring as well as synthetic fragments is disclosed. These synthetic analytes are reasonably interpreted as being within the analyte scope of the instant claims because they are not "cell fixed *in situ*" type as negated in the above listed instant claims. Both covalent and non-covalent fixation of single stranded polynucleotide is cited in column 3, lines 31-40, inclusive also of glass slides which are reasonably interpreted as the commonly utilized non-porous microscope type slides which are well known in the art. Said column 3, lines 31-40, citation also includes disclosure of surface treatment as in instant claim 3151, for example. RNA probes which hybridize to said sample single-stranded nucleic acids are disclosed in column 3, lines 10-21. Antibody detection complexes including non-radioactive labels for detection of hybridized DNA-RNA hybrids are described in column

Art Unit: 1631

4, lines 24-55. Thus, the instant claims directed to hybridizable nucleic acids on a non-porous support wherein

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (571) 272-0718. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 19, 2004

Ardin H. Marschel 11/22/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER